



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,061	03/09/2005	Oliver May	266811US0XPCT	4748

22850 7590 10/27/2006

C. IRVIN MCCLELLAND
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER

MEAH, MOHAMMAD Y

ART UNIT	PAPER NUMBER
----------	--------------

1652

DATE MAILED: 10/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/527,061	MAY ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/5/05</u> | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1652

DETAILED ACTION

Claims 1-9 are pending in the instant office action for examination. With the response filed 8/13/2006, the applicant elected with traverse Group I (claims 1-5) for further examination

Election/Restriction

During preliminary amendment of this application, the applicant, on date 8/13/2006 elected with traverse Group I (claims 1-5), drawn to recombinant microorganism for preparation of D-amino acids.

Applicant's election with traverse of group I (claims 1-5) in the reply filed on 08/13/2006 is acknowledged.

The traversal is on the ground(s) that unity exists between the claims and therefore restriction was not proper. Applicant's arguments have been fully considered and found persuasive and therefore groups II claims (claims 6-9 will be examined with group I claims.

Priority

Acknowledgement is made of applicant's PCT priority date based on application filing date of 10/15/2003 of PCT/EP03/11432 and foreign applications Germany 102-51-184.5 filed on date 11/04/2002.

Claim Rejections**35 U.S.C 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a genus of recombinant microorganisms comprising genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any mutagenesis from any source. While claims 2-3 are directed to recombinant *E. coli* comprising genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any mutagenesis. The specification teaches the structure of only a few representative species of such recombinant microorganisms. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than efficient production of D-amino acids and the lack of D-amino acid oxidase and/or D-serine dehydratase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would

Art Unit: 1652

recognize that applicants were in possession of the claimed invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific recombinant microorganism (such as *E. coli* DSM 15181 or DSM 15182) having inactivated D-amino acid oxidase and/or D-serine dehydratase by deleting genes of D-amino acid oxidase and/or D-serine dehydratase of SEQ ID NO: 5 or 6; and/ or SEQ ID NO: 7 or 8 and method of production of D-amino acid using said recombinant microorganisms does not reasonably provide enablement for any recombinant microorganisms comprising any genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any method of mutagenesis and method of production of D-amino acid using said recombinant microorganisms. There are many ways genes of D-amino acid oxidase and/or D-serine dehydratase in a microorganisms can be inactivated such as deletion, substitution of specific amino acid residues of DNA sequence of the D-amino acid oxidase and/or D-serine dehydratase or deletion of the whole genes, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-9 are so broad as to encompass any recombinant microorganism with genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any means and method of production of D-amino acid using said recombinant microorganisms. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to any recombinant microorganism with genes of D-amino acid oxidase

Art Unit: 1652

and/or D-serine dehydratase inactivated by any means broadly encompassed by the claims.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to inactivation of few genes encoding mutated D-amino acid oxidase and/or D-serine dehydratase .

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass microorganisms comprising wherein microorganisms D-amino acid oxidase and/or D-serine dehydratase are inactivated by any method of mutagenesis and method of production of D-amino acid using said recombinant microorganisms because the specification does not establish: (A) regions of the protein structure which may be

Art Unit: 1652

modified to eliminate D-amino acid oxidase activity (B) the general tolerance of modification and extent of such tolerance on D-amino acid oxidase and/or D-serine dehydratase; (C) a rational and predictable scheme for modifying any D-amino acid oxidase and/or D-serine dehydratase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any recombinant microorganisms comprising containing genes of D-amino acid oxidase and/or D-serine dehydratase inactivated by any method of mutagenesis and method of production of D-amino acid using said recombinant microorganisms. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of oxidoreductase variants, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir,1988).

CLAIM Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1652

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3 and 6-9 are rejected under 35 U.S.C. 103(a) by Altenbuchner et al. (US 6800464) in view of Marceau (JBC 1988, PP 16916-16933)

Altenbuchner et al. (US 6352848) teach recombinant microorganisms (such as *E.coli*,) expressed with hydantoins racemase and D- carbamoylase genes from *Arhrobacter* and methods of production D-amino acids using said recombinant microorganism.

Marceau et al. (JBC 1988, PP 16916-16933) teach the isolation of D-serine dehydratase (DSD) from *E.Coli* and found that inactivating DSD in *E. coli* by mutating amino acid residues of DSD polypeptide decrease the degradation of D-amino acids (such as D serine, D-threonine, etc).

A skilled artisan would understand that elimination or deletion D-serine dehydratase (DSD) in *E. coli* would increase the accumulated D-amino acid produce by *E.coli*, expressed with hydantoins racemase and D- carbamoylase genes because D-amino acid would not be degraded by DSD.

As such it would have been obvious to one of ordinary skill in the art to use the microorganism taught by Altenbuchner et al. and modify the microorganism by deleting

Art Unit: 1652

or mutating the DSD gene as suggested by Marceau et al. to increase the production of D-amino acid.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Application/Control Number: 10/527,061

Page 9

Art Unit: 1652


Mohammad Younus Meah, PhD

Examiner, Art Unit 1652

Recombinant Enzymes, 3C31 Remsen Bld

400 Dulany Street, Alexandria, VA 22314

Telephone: 517-272-1261


REBECCA E. PRO CUTY
PRIMARY EXAMINER
GROUP 1652
1600